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### Remarks

Reconsideration and withdrawal of the objections to the specification and rejections of the claims in the Office Action dated September 26, 2003, in view of the amendment and remarks herein and the Amendment filed on December 23, 2003, is respectfully requested. Claims 1-34 are now pending in this application.

The specification is amended at page 8, thereby addressing the Examiner's objection to the specification at page 2 of the Office Action.

In the Advisory Action, the Examiner asserts that only the last 13 residues of P3 correspond to residues in engrailed. Figure 2 in the present specification provides the sequence of P3, which has 33 residues, and indicates which residues in the sequence are from engrailed (double underline) or EF-hand (single underline), i.e., TERRRQQLDKDGDGTI DERE IKIHFQNKRAKIK. For the Examiner's convenience, a copy of NCBI Accession No. NP-001417, which discloses a human engrailed amino acid sequence, is provided herewith in which the sequences in P3 corresponding to the engrailed homeodomain are underlined. The homeodomain in the engrailed sequence in NCBI Accession No. NP-001417 corresponds to residues 303 to 362. Thus, the homeodomain in the engrailed sequence in NCBI Accession No. NP-001417 has 60 residues, and the first 8 residues of P3, i.e., TERRRQQL, correspond to residues 27 (residue 27 is a threonine) to 34 (residue 34 is a leucine), i.e., T<sub>27</sub>-L<sub>34</sub>, in engrailed, and the last 16 residues of P3, i.e., ERE...KIK, correspond to residues 42 (residue 42 is a glutamic acid) to 57 (residue 57 is a lysine), i.e., E<sub>42</sub>-K<sub>57</sub>, in engrailed (page 9, lines 1-2 and page 50, lines 25-28).

Moreover, the residue at the position in P3 corresponding to position 43 in a homeodomain is disclosed as the residue at position 43 in the Antennapedia homeodomain, i.e., R (see NCBI Accession No. P02833; a copy was provided with the Amendment filed on December 23, 2003). The homeodomain in the engrailed sequence in NCBI Accession No. P02833 includes 60 residues corresponding to residues 297 to 356, and residue 43 in that homeodomain is R, i.e., R<sub>43</sub>. Thus, the numbering in Applicant's specification adequately describes and enables the claimed invention.

Accordingly, withdrawal of the § 112(1) rejections is respectfully requested.

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612) 373-6959 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.


Respectfully submitted,

SONYA FRANKLIN,

By her Representatives,

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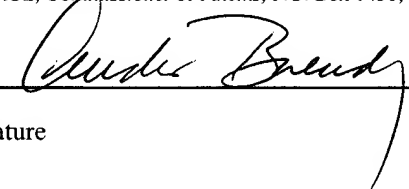
Date February 26, 2004

By   
Janet E. Embretson  
Reg. No. 39,665

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☐ 1: NP\_001417. engrailed homolog...[gi:7710119]

BLink, Domains, Links

LOCUS NP\_001417 392 aa linear PRI 04-OCT-2003  
DEFINITION engrailed homolog 1 [Homo sapiens].  
ACCESSION NP\_001417  
VERSION NP\_001417.2 GI:7710119  
DBSOURCE REFSEQ: accession NM\_001426.2  
KEYWORDS  
SOURCE Homo sapiens (human)  
ORGANISM Homo sapiens  
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.  
REFERENCE 1 (residues 1 to 392)  
AUTHORS Loomis,C.A., Harris,E., Michaud,J., Wurst,W., Hanks,M. and Joyner,A.L.  
TITLE The mouse Engrailed-1 gene and ventral limb patterning  
JOURNAL Nature 382 (6589), 360-363 (1996)  
MEDLINE 96300324  
PUBMED 8684466  
REFERENCE 2 (residues 1 to 392)  
AUTHORS Kohler,A., Logan,C., Joyner,A.L. and Muenke,M.  
TITLE Regional assignment of the human homeobox-containing gene EN1 to chromosome 2q13-q21  
JOURNAL Genomics 15 (1), 233-235 (1993)  
MEDLINE 93162666  
PUBMED 8094370  
REFERENCE 3 (residues 1 to 392)  
AUTHORS Logan,C., Hanks,M.C., Noble-Topham,S., Nallainathan,D., Provart,N.J. and Joyner,A.L.  
TITLE Cloning and sequence comparison of the mouse, human, and chicken engrailed genes reveal potential functional domains and regulatory regions  
JOURNAL Dev. Genet. 13 (5), 345-358 (1992)  
MEDLINE 93185339  
PUBMED 1363401  
REFERENCE 4 (residues 1 to 392)  
AUTHORS Logan,C., Willard,H.F., Rommens,J.M. and Joyner,A.L.  
TITLE Chromosomal localization of the human homeo box-containing genes, EN1 and EN2  
JOURNAL Genomics 4 (2), 206-209 (1989)  
MEDLINE 89290849  
PUBMED 2567700  
COMMENT REVIEWED REFSEQ: This record has been curated by NCBI staff. The reference sequence was derived from [L12699.1](#). On May 5, 2000 this sequence version replaced [gi:4503567](#).

Summary: Homeobox-containing genes are thought to have a role in controlling development. In Drosophila, the 'engrailed' (en) gene plays an important role during development in segmentation, where

it is required for the formation of posterior compartments. Different mutations in the mouse homologs, En1 and En2, produced different developmental defects that frequently are lethal. The human engrailed homologs 1 and 2 encode homeodomain-containing proteins and have been implicated in the control of pattern formation during development of the central nervous system.

FEATURES

Location/Qualifiers

source 1..392  
/organism="Homo sapiens"  
/db\_xref="taxon:9606"  
/chromosome="2"  
/map="2q13-q21"

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/product="engrailed homolog 1"

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Region 305..360  
/region\_name="Homeobox domain"  
/note="homeobox"  
/db\_xref="CDD:pfam00046"

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go\_function: transcription factor activity [goid 0003700] [evidence IEA];  
go\_process: skeletal development [goid 0001501] [evidence TAS] [pmid 8684466];  
go\_process: embryogenesis and morphogenesis [goid 0007345] [evidence TAS] [pmid 8094370];  
go\_process: regulation of transcription, DNA-dependent [goid 0006355] [evidence IEA];  
go\_process: development [goid 0007275] [evidence IEA]"  
/db\_xref="GeneID:2019"  
/db\_xref="LocusID:2019"  
/db\_xref="MIM:131290"

## ORIGIN

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